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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,672	02/07/2001	Hsu Ching-Hsaing	12774-002001	4367

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EXAMINER

LI, QIAN J

ART UNIT	PAPER NUMBER
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1632

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DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/778,672

Applicant(s)

CHING-HSAING ET AL.

Examiner

Q. Janice Li

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 July 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment.
6. ☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 24-33, 35-39 and 41-49.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

ANNE M. WEHBE' PH.D.  
PRIMARY EXAMINER

Attachment to Box 5.

The amended claims 24 and 43 added the limitation, "wherein the promoter is functional in the non-pathogenic, Gram-positive bacterium", and "expressing the allergen in the non-pathogenic, Gram-positive bacterium". These limitations could be found in the teaching of Medaglini et al, who teach a system allowing the stable expression of a wide range of protein antigens on the surface of non-pathogenic, Gram-positive commensal bacterium (abstract), the promoter in the pSMB-7 is apparently functional in the non-pathogenic, Gram-positive bacterium. The amended claims 36 and 44 added the limitation, "expressing the allergen in the lactic acid bacterium while the lactic acid bacterium is in the subject". Casas et al and Kailasapathy et al teach expressing heterologous protein in the lactic acid bacterium after they are administered to a subject (vaccine delivery vehicle).

In paper #20, applicants only presented arguments to US patent 5,958,891 and Medaglini reference, which in addition to reiterating the previous arguments, relied mostly on the newly submitted Declaration of Dr. Hsu.

In response, first, applicants are reminded that the Declaration has not been considered because this rejection has been on record since the first action on merit (Paper #13). Second, regarding Medaglini's system, as indicated in Paper# 18, it is a general system for delivering broad range of proteins in an individual and inducing immune response of the host to the expressed protein. The working example is expressing and inducing immune response to an allergen. The system is an alternative

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for direct nucleic acid delivery. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, *Hsu et al* teach a method for treatment of allergy by delivering an allergen to a host via direct injection of a nucleic acid expressing the allergen, and *Medaglini et al* teach another means of delivering an allergen to a host by using a non-pathogenic Gram-positive commensal bacteria expressing an allergen. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Hsu et al*, by simply substituting the nucleic acid construct with the bacteria expression system with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because oral dosing is more practical in clinical vaccination. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Therefore, the rejections stand.